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In Memoriam

In memory of Dr. John Saunders

Dr. John W. Saunders, Jr., an eminent developmental biologist whose pioneering experiments helped elucidate the tissue interactions controlling vertebrate limb patterning, passed away peacefully on December 26th at the age of 96. Saunders was recognized for both his outstanding research contributions to the field of developmental biology, as well as for his excellence and enthusiasm as an educator. His many discoveries remain central to our understanding of the development of the vertebrate limb. Particularly notewothy were his studies of the apical ectodermal ridge (AER), which helped identify the role of growth factors in patterning the developing limb, and his identification of the zone of polarizing activity (ZPA) and studies demonstrating its role in anterior–posterior limb patterning. His early recognition of the role of cell death in development and analyses of feather patterns are also part of his impressive scientific legacy.

Born in Muskogee, Oklahoma, on November 12, 1919, Saunders' childhood was marked by poverty following a fire that destroyed his father's barbershop, the family's sole means of livelihood. Saunders began work at age 8 and by age 13 was working after school from 4:00 to 10:00 PM six days a week (Fallon, 2002). All his wages went to help feed the family. Despite his family's financial situation, Saunders' combination of a strong work ethic, natural intelligence and a good measure of luck brought him to the attention of a state senator who promised him a job—and therefore the funds for college—if Saunders could teach his son enough French to pass an exam.

His success in that endeavor provided the stepping stone to a higher education, first at the University of Oklahoma, Norman, where he received a B.S. in Zoology in 1940 and an M.S. in Zoology in 1941, and then at Johns Hopkins University where he earned his Ph.D. in 1948.

At Hopkins, Saunders studied feather organization and polarity in the chick embryo with Dr. Benjamin Willier. Trained by Mary E. Rawles, he used microsurgery and transplantation techniques to explore the effects of altering tissue orientation on the developing embryo. His studies were interrupted though in 1943 when he enlisted in the Navy and served as Lieutenant on the U.S.S. Rocky Mount in the Pacific theater during World War II. In 1946, at the war's end, he returned to Hopkins to complete his research.

While watching one of Saunders' transplantation experiments, Willier noticed that the dye Saunders used to track his grafts also stained an ectodermal thickening on the apex of the limb bud (Fallon, 2002). Curious about this structure now called the apical ectodermal ridge, Saunders removed it at various stages of development and found it resulted in a truncated wing. In fact, the earlier in development it was excised, the more truncated the wing was. This became the focus of his thesis which culminated in a 1948 paper published in *The Journal of Experimental Zoology* (Saunders, 1948). Saunders showed that the AER is essential for the outgrowth of the limb bud and that limb structures form temporally in a proximodistal manner with more distal structures developing later. The significance of Saunders' work was recognized immediately by Paul Weiss, a leader in the field of developmental biology who Saunders recalled stood up at an American Society of Zoologists meeting in 1947and declared, "Ladies and gentleman, this is the most significant finding in the field of developmental biology in the last fifty years" (Tyler et al., 2003). It would be another fifty years before the molecules that induce and maintain the AER—fibroblast growth factors—were identified.

Following a post-doctoral appointment with Paul Weiss at the University of Chicago, Saunders taught at Marquette University in Milwaukee, WI, eventually becoming chairman of the Department of Biology. There he began to study cell death in the developing limb bud with Mary Gasseling (Saunders and Gasseling, 1962). While conducting transplantation experiments in which they grafted regions of limb mesenchyme that were undergoing cell death to other regions of the limb bud, they stumbled upon what they named the zone of polarizing activity (Saunders and Gasseling, 1968). The ZPA is a region of mesenchyme that sits at the posterior edge of the limb bud. When it was transplanted to an anterior location under the AER of another limb bud, an ectopic mirror image limb formed in the embryo. Subsequent experiments

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showed that the ectopic wing always formed with its posterior side facing the graft site. Saunders' group had thus discovered the source of the signal that determined anteroposterior axis polarity in the limb. *Sonic hedgehog* was identified twenty-five years later by Cliff Tabin's group as the polarizing factor in the ZPA (Riddle et al., 1993).

After a year at the University of Pennsylvania as Professor of Anatomy, Saunders was appointed Professor of Biological Sciences at the State University of New York at Albany in 1967 where he remained until 1985 when he became Professor Emeritus.

Deeply involved in the scientific community Saunders was a longtime member of many scientific societies including the American Association for the Advancement of Science and the American Association of Anatomists. Between 1959 and 1966 he served several leadership roles at the American Society of Zoologists including chair of the developmental biology division and secretary. From 1967 to 1968 he served as president of the Society for Developmental Biology.

Summer research and teaching opportunities took him to the Mount Desert Island Biological Laboratory in Salisbury Cove, ME in 1954 and then to the Marine Biological Laboratory in Woods Hole, MA, where he was a summer investigator from 1958 to 1972. From 1995 to 2003, he was a lecturer in the Embryology Course at the MBL, where he continued to inspire many young developmental biologists.

Saunders was the recipient of numerous awards during his distinguished career, including the Edwin Grant Conklin Medal by the Society for Developmental Biology in 1996 and the University of Oklahoma College of Arts and Sciences Distinguished Alumni Award in 2007. Saunders was elected to the National Academy of Sciences in 2006.

Dr. John Fallon, a former student and colleague of Saunders reflected on the scientific impact of his work. “I sat and thought about what characterized his career. What came to me first was his personal integrity in his approach to his life and his loyalty to his colleagues. His lifelong conversation with the developing embryo was the joy in his professional life. One way or another, his published work is a foundation for much of the current molecular and cellular understanding of pattern formation. Thus, over the decades the words change for continuing the conversation with the embryo. However, the basic foundation of John Saunders scientific legacy remains.”

Saunders is survived by his children: Sarah Elizabeth Reeder of Baltimore, MD; Jack Saunders of Mt. Shasta, CA; Maggie Geist of North Falmouth, MA; and Kitty Brown of East Falmouth, MA; his sister, Virginia Lavarine of Fleming Isle, FL; seven grandchildren, seven great-grandchildren and numerous nieces and nephews. He was predeceased by his son, William Michael Saunders, a grandson, Danny Brown, and his wonderful wife of 69 years, Lilyan C. Saunders who died in 2011.

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